

Problem Set 8
Genetics 371
Winter 2010

1. In a population exhibiting Hardy-Weinberg equilibrium, 23% of the individuals are homozygous for a recessive character. What will the genotypic, phenotypic and allelic frequencies be for the next generation?

Let's call the recessive allele "r" and the dominant allele "R". The allele and genotype frequencies in the next generation are:

$r = 0.48$
 $R = 0.52$
 $RR = 0.27$
 $Rr = 0.50$
 $rr = 0.23$

The frequency of the recessive character will therefore be 23% in the next generation.

2. Red hair (autosomal recessive) is found in approximately 4% of people in Norway. If we assume that the Norwegian population is in Hardy-Weinberg equilibrium,

(a) What are the frequencies of the red hair (r) and the non-red hair (R) alleles?

$R = 0.8, r = 0.2$

(b) What is the frequency of heterozygotes?

0.32

(c) What proportion of all marriages stand a chance of having a child with red hair?

Marriages of either $rr \times rr$ or $Rr \times Rr$ can produce a child with red hair. The frequency of the first type of mating is $r^2 * r^2$ and the frequency of the second mating is $2Rr * 2Rr$. Therefore, the total proportion of all marriages with a chance of producing a red haired child is $r^4 + 4R^2r^2$.

3. A particular early-onset, form of cancer in humans was mapped to two genes, CA18 and CA19, located on chromosomes 14 and 9, respectively. A new extended family showing inheritance of this same form of cancer was recently detected. A small portion of the pedigree is shown on the next page, and the results from LOD score analysis using this family is shown in the table below.

Polymorphic site	LOD score for $\theta = 0.05$
D14S16 (tightly linked to CA18)	-2.92

D9S722 (tightly linked to CA19)	-3.01
D12S1030 (on chromosome 12)	6.24

(a) What is the likely mode of inheritance of this cancer predisposition (autosomal or sex-linked; recessive or dominant)?

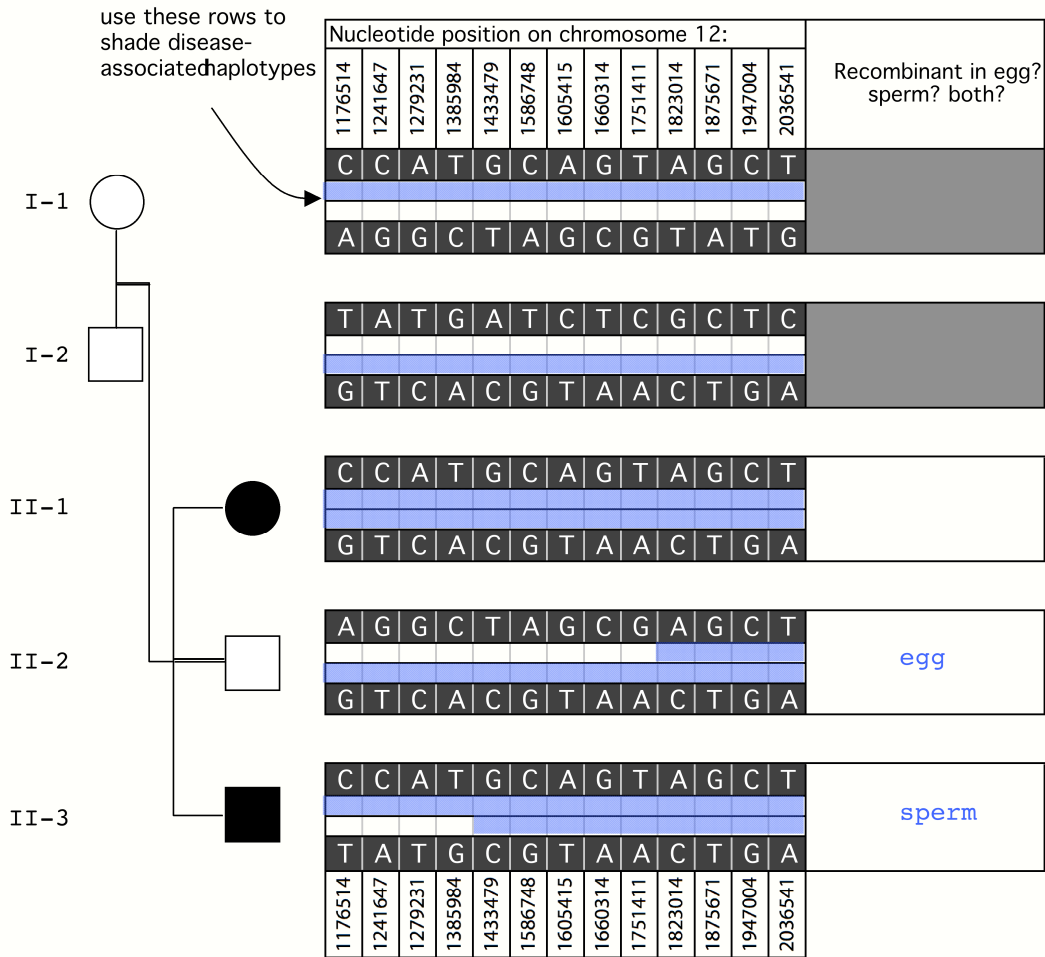
Likely autosomal, recessive; two unaffected parents have a son and a daughter with the cancer predisposition.

(b) Why did these LOD score results prompt the researchers to begin a search for yet another cancer gene?

Evidence against linkage to known loci (LOD scores below -2.0) and strong evidence for linkage at a new locus (LOD > +3.0 on chromosome 12) suggest that another gene is in play.

(c) To map this new gene (called CA20), the researchers genotyped members of this extended family by hybridizing their DNA samples to allele-specific oligonucleotide microarrays. The genotyping results for DNA flanking marker D12S1030 on chromosome 12 are shown to the right of each member in the pedigree. Filled pedigree symbols = affected individuals. Each row represents one haplotype; only the Watson strand base is shown at each single-nucleotide polymorphic locus.

- For each parent, identify each disease-bearing homologue by shading its haplotype. (Use the center blank rows for each individual to show your shading.)
- For each child, shade part or all of each homologue as necessary to indicate recombinant vs. non-recombinant haplotypes. Indicate the recombinant gamete, if any: egg, sperm, or both.



(d) Circle the option below that best represents the location of CA20:

Between 1176514 and 2036541

Between 1433479 and 1751411

Between 1385984 and 1823014

Between 1433479 and 2036541

(e) Postulate a mechanism that results in early onset cancer that is consistent with your mode of inheritance.

This is a hard, thought question that we haven't considered in class or quiz section. A recessive cancer-predisposing mutation would likely be in a tumor suppressor gene since both copies have to be inactivated. That inheritance doesn't show a dominant pattern (like BRCA1 mutation) might suggest low penetrance of the single mutation, with only a small risk of early onset cancer, but high penetrance when all cells of a woman from birth have no active gene product from this locus.

4. A breeding experiment was performed on pure lines of tomatoes differing in fruit weight. The plants were all grown in a controlled environment chamber providing equal environmental conditions for all individuals as far as humanly possible. The results were as follows:

Parental lines	A 24 g	x	B 32 g
F1	28 g		
F2	<u>Weight (g)</u>	<u>Number of plants</u>	
	36	2	
	34	14	
	32	60	
	30	108	
	28	140	
	26	114	
	24	52	
	22	18	
	20	2	

Show how a polygene model can explain these results, and give

(a) A general statement of your model (how many loci and whether alleles are additive, dominant, or recessive).

The phenotypic distribution is consistent with 4 additive loci (recall that the number of possible phenotypic classes in this model is $2n+1$; thus $2n + 1 = 9$ and $n = 4$).

(b) Genotypes of the parents and F1.

Parents: AABBCDD and aabbccdd
 F1: AaBbCcDd

(c) The effect of each “active” allele on the phenotypic value.

The effect of each “active” allele is to add 2 grams of weight. Note that the range of values of the F2 is different than what is seen in the parents. This is a common phenomenon for quantitative traits (technically referred to as transgressive segregation) and can result from epistatic interactions. Note – the intention was to make you think about possible ways in which the results above could be obtained and we won’t be asking any questions about transgressive segregation on the final.

(d) Explain the frequencies of the 20 g and the 36 g F2 classes

These are the least abundant genotypic classes (20 g = aabbccdd and 36 g = AABBCCDD) that result from a fully heterozygous cross (i.e., AaBbCcDD x AaBbCcDd).

5. In Friday's class, we discussed a statistic to quantify population genetic structure. What is it and how do you interpret it?

The statistic F_{ST} is used to quantify population structure. Essentially it is a measure of how much allele frequency variation there is between populations. For example, in humans $F_{ST} = 0.123$, which means that approximately 12% of genetic variation in humans is due to differences between populations and 88% ($1 - F_{ST}$) is due to differences among individuals within populations. Thus, the vast majority of genetic variation in humans is due to differences between individuals rather than populations.